



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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31,591,441 04/18/96 QUENTIN MILLET

M XI/P02958US0

EXAMINER

18N2/0514

THOMAS F. SWORD
LARSON & TAYLOR
727 23RD STREET SOUTH
ARLINGTON VA 22202

PART UNIT	PAPER NUMBER
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1812

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DATE MAILED: 05/14/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|--|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input checked="" type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input checked="" type="checkbox"/> <u>NOTICE TO COMPLY SERVICE RULES.</u> |

Part II SUMMARY OF ACTION

1. ☒ Claims 54-82 are pending in the application.
Of the above, claims 79-82 are withdrawn from consideration.
2. ☒ Claims 1-53 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 54-78 are rejected.
5. ☐ Claims _____ are objected to.
6. ☒ Claims 54-82 are subject to restriction or election requirement.
7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☒ been filed in parent application, serial no. PCT/EP95/0801; filed on 5-30-95.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

1. The preliminary amendments filed 18 April 1996, Paper No. 6, and filed 7 February 1997, Paper No. 13, have been entered.

Election/Restriction

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 54-78, drawn to a polypeptide, an isolated DNA fragment, and a pharmaceutical composition of polypeptide.

Group II, claim(s) 79-82, drawn to monoclonal antibody and a pharmaceutical composition of antibody.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons.

Group I is drawn to a polypeptide, an isolated DNA

fragment, and a pharmaceutical composition of polypeptide.

Pursuant 37 CFR 1.475(d), these claims are considered by the ISA/US to constitute the main invention, and none of the related group II correspond to the main invention.

The products of Groups I and II do not share the same special technical features because any one of the product of group I and II are structurally and functionally different from each other and each defines a separate invention over the art.

During a telephone conversation with Attorney Thomas Sarro on 29 April 1997 a provisional election was made with traverse to prosecute the invention of I, claims 54-78. Affirmation of this election must be made by applicant in responding to this Office action. Claims 79-82 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37

CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Priority

3. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Specification

4. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the title of the invention, each of the lettered items should be preceded by the headings indicated below.

- (a) Title of the Invention.
- (b) Cross-References to Related Applications (if any).
- © Statement as to rights to inventions made under Federally-sponsored research and development (if any).
- (d) Background of the invention.
 - 1. Field of the Invention.
 - 2. Description of the Related Art including information disclosed under 37 CFR 1.97-1.99.
- (e) Summary of the Invention.
- (f) Brief Description of the Drawing.
- (g) Description of the Preferred Embodiment(s).
- (h) Claim(s).
- (I) Abstract of the Disclosure.

The heading for the Brief Description of the Drawing is missing from page 19, line 10.

Sequence Rules 37 CFR 1.821-1.825

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures.

Page 30, lines 36 and 39 disclose an amino acid sequence of peptides which must comply with the sequence rules.

Applicant is given the period set for response to this Office action from the date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for response beyond the SIX MONTH statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

6. The specification is objected to because it does not comply with 37 C.F.R. 1.821 (d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification wherever a reference is made to that sequence. See M.P.E.P. 2422.04.

The legends for figures 1-4 and 8-10 (on page 19, lines 12-35) must identify each of the sequences disclosed in figures 1-4 and 8-10 with the individual SEQ ID NO:. It is not sufficient to identify the sequence as a fragment of larger SEQ ID NO: because

each sequence disclosure has its own SEQ ID NO:. Pages 20, 24, and 30 also disclose sequences which must be identified by its SEQ ID NO:. Any references to sequences in the specification or the claims must be identified with an appropriate SEQ ID NO:.

Claim Rejections - 35 USC § 112

7. Claims 54-78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Tbp2 receptor of SEQ ID NO:2 and 4, does not reasonably provide the full scope of enablement for derivatives of Tbp2 receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 54-78 encompass Tbp2 derivatives and variants because of the recitation of an "derived". However, the specification fails to teach how to use the derivatives of Tbp2 because the claims are single means claims. A single means claim is a claim which depend on a recited property, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those

known to the inventor (MPEP 2164.08(a)). The specification defines on page 7, lines 36-39, that the term "sequence which is derived from another sequence" to mean a sequence originating from this other sequence by the use of a mental process. Thus, the claims encompass all variants of Tbp2 based on sequence comparisons and mental processes. One skilled in the art cannot predict whether such polypeptides would have any relationship to the TBP2 polypeptide. The state of the art is such that one skilled in the art cannot predict the tertiary structure of protein based on the primary amino acid sequence (Bowie et al.(S)). Thus, it would require undue experimentation to make and use variants with amino acid substitutions in the Tbp2 receptor because one skilled in the art could not predict the effect of the changes due to substitutions on the tertiary structure of the Tbp2 receptor which is necessary to determine if the protein is functional. Furthermore, changes tertiary structure will affect any antibody based on the original epitope of the natural Tbp2 protein found in the bacteria and if the antibody does not recognize the natural Tbp2 protein in the bacteria it cannot be used in diagnostic assay or for vaccination. It would require empirical determination to

determine the all variant combinations which are functional because one skilled in the art cannot predict the which combination of variants of Tbp2 receptor would result in a functional polypeptide. Guidance and working examples directed to the Tbp2 receptor in the specification are not predictive of using any variants or derivatives of Tbp2 receptor because the changes in tertiary structure affects the protein function in an unpredictable manner. Therefore, in view of the large extent and unpredictable nature of the experimentation which would be involved, one skilled in the art could not make and use the full scope of the invention as claimed without undue experimentation.

8. Claims 54-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A deposit of the Neisseria meningitidis strain IM2169 or IM2394 is required to enable the invention of claims 54-78. This determination has been made because the claimed strains or vectors have not been fully disclosed or the materials required

to isolate the claimed strains have not been shown to be publicly known and fully available. The specification does not teach how to make the disclosed strains, in a sufficient manner to practice the invention because one skilled in the art could not determine the exact materials necessary to construct the strains. It would require undue experimentation to determine the exact materials necessary to construct the strains. Without a publicly available deposit of the above vectors or strains, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. A suitable deposit for patent purposes is required.

If a deposit has been made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating (a) that the deposit has been made under the terms of the Budapest Treaty; and (b) that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then the requirements may be satisfied by an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or by a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and establishing that the following criteria have been met: (a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto; (b) all restrictions imposed by the

depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; (c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material; (d) a viability statement in accordance with the provisions of 37 C.F.R. § 1.807 is provided; and (e) the deposit will be replaced should it become necessary due to inviability, contamination, or loss of capability to function described in the manner in the specification.

In either case, the identifying information set forth in 37 C.F.R. § 1.809(d) should be added to the specification if it is not already present. See 37 C.F.R. §§ 1.803-1.809 for additional explanation of these requirements.

9. Claims 54-78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 54-78 is indefinite for recitation of "stringent conditions" which is a relative term and it is not clear whether the condition is high, moderate, or low stringency condition for hybridization.

Claims 54-78 are indefinite and confusing because SEQ ID NO:1 and 3 are DNA sequences and the claims are to polypeptide thus it is not clear how a maximal homology alignment can be performed between a DNA sequence and an amino acid sequence.

Claims 54-78 are indefinite and confusing because of the

recitation of "maximal homology alignment". The instructions or algorithm for determining sequence identity is missing from the specification. Furthermore, the metes and bounds of the term "homology" have not been clearly set forth neither in the claims nor in the specification. The precise meaning of "homology" in biology is having a common evolutionary origin" (Reeck et al.; R). The paper further explains that homology is a concept of quality or type of relationship between two or more things. Thus, amino acids or nucleotide sequences cannot exhibit a particular quantity or level of homology or percent homology. A more appropriate term is "identity." However, it should be noted that quantitative determination of identity requires subjective determinations for sequences compared. Thus, a specific definition of "identity" must be defined taking into considerations such variables as: complete vs partial sequence and gap distances.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 54-77 rejected under 35 U.S.C. 102(b) as being anticipated by Legrain et al. (AS).

Legrain et al. disclose the Tbp2 protein and DNA sequence from *Neisseria meningitidis* strains B16B6 and M982 (page 74, Results...; page 76, figure 2; page 78, figure 4). Legrain et al. disclose the tryptic peptide fragments of Tbp2 protein (page 74, paragraph bridging the left and right columns).

The examiner has assumed that SEQ ID NO: 1 and 3 should have been directed to the encoding protein amino acid of SEQ ID NO: 2 and 4. Although not called IM2169 and IM2394, the strains M982 and B16B6 are the same. SEQ ID NO: 2 and 4 are identical to the TBP2 amino acid sequences of Legrain et al. (see attached sequence comparisons). The term "derived" is construed to encompass variants and derivatives.

12. Claims 54-76 and 78 are rejected under 35 U.S.C. 102(b) as being anticipated by Quentin-Millet et al. (AM).

Quentin-Millet et al. disclose the pharmaceutical vaccine

composition comprising Tbp2 protein from Neisseria meningitidis strains 2169 and 2394 (see abstract).

The examiner has assumed that SEQ ID NO: 1 and 3 should have been directed to the encoding protein amino acid of SEQ ID NO: 2 and 4. Although not called IM2169 and IM2394, the strains 2169 and 2394 are the same. The term "derived" is construed to encompass variants and derivatives. The Tbp2 receptor inherently has the amino acid sequence of SEQ ID NO:2 and 4 because Tbp2 receptor of Quentin-Millet et al. is the same receptor as claimed.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Quentin-Millet et al.(AN), Stevenson et al.(AR), and Jacobs et al.(AL), is cumulative reference with Quentin-Millet et al.(AM).

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Pak whose telephone number is (703) 305-7038. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephen Walsh, can be

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reached on (703) 308-2957. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

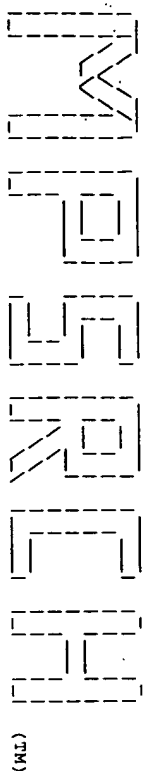
MOP

Michael D. Pak

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29 April 1997

Stephen Walsh
STEPHEN WALSH
SUPERVISORY PATENT EXAMINER
GROUP 1800



Release 2.1D John F. Collins, Biocomputing Research Unit.
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Search: protein - protein database search, using Smith-Waterman algorithm
Date: Wed Apr 23 08:05:58 1997; Maspar time 24.91 Seconds
813,564 Million cell updates/sec
Tabular output not generated.

Title: >US-08-591-447-2
Description: (1-711) from US08591447.ppt
Perfect Score: 4803
Sequence: 1 MNPLVNOAAVLPVFLLSA.....GNSASATVFGAKRQDPVQ 711

Scoring table: PAM 150
Gap 11

Searched: 89912, seqs, 28507787 residues
Post-processing: Minimum Match 0%
Listing first 45 summaries

Database:

1:unani 2:ann2 3:ann3 4:ann4 5:unani1 6:unani2 7:unani3
8:unani4 9:unani5 10:unani6 11:unani7 12:unani8
13:unani9 14:unani10 15:unani16:unani17

Statistics: Mean 49.273; Variance 110.985; scale 0.444

Pred. No. is the number of results predicted by chance to have a
score greater than or equal to the score of the result being printed,
and is derived by analysis of the total score distribution.

SUMMARIES

Result	No.	Score	Query	Match	Length	DB	ID	Description	Pred. No.
1	4803	100.0	711	7	JN0820	transferrin-binding	0.00e+00		
2	1208	25.2	216	16	S61545	transferrin-binding	3.11e-191		
3	1202	25.0	210	16	S61548	transferrin-binding	4.02e-191		
4	1062	22.1	213	16	S61549	transferrin-binding	3.00e-164		
5	1045	21.8	217	16	S61546	transferrin-binding	4.07e-161		
6	766	15.9	599	7	JN0818	transferrin-binding	3.93e-110		
7	612	12.7	625	9	D64107	transferrin-binding	1.82e-82		
8	491	10.2	216	16	S61544	transferrin-binding	3.99e-61		
9	469	9.8	593	9	B44796	transferrin-binding	2.69e-57		
10	468	9.8	593	9	S27483	transferrin-binding	2.69e-57		
11	448	9.3	547	9	S49814	transferrin-binding	1.16e-53		
12	420	8.7	547	9	A44796	transferrin-binding	7.62e-49		
13	403	8.4	547	9	S49815	transferrin-binding	6.13e-46		
14	276	5.7	41	7	S37626	transferrin-binding	2.40e-25		
15	129	2.7	660	1	ALBS	alpha-amylose (EC 3.	2.67e-03		
16	127	2.6	477	5	S02098	alpha-amylose (EC 3.	4.73e-03		
17	125	2.6	477	5	A36709	alpha-amylose (EC 3.	8.32e-03		
18	124	2.6	477	1	ALBSN7	alpha-amylose (EC 3.	1.10e-02		
19	127	2.6	592	1	ALBSNA	alpha-amylose (EC 3.	4.73e-03		
20	113	2.4	35	16	S61547	transferrin-binding	2.21e-01		
21	110	2.3	127	3	R7SMG	ribosomal protein L1	4.87e-01		

22	111	2.3	835	3	A45596	trypanastigote-speci	3.75e-01
23	110	2.3	1054	11	A30239	hydroxymethylglutary	4.87e-01
24	106	2.2	127	7	S49537	ribosomal protein L1	1.36e+00
25	105	2.2	320	5	S59947	chitinase (EC 3.2.1.	1.75e+00
26	106	2.2	370	16	S60187	peridinin-chlorophyll	1.36e+00
27	107	2.2	386	1	CTWMS	site-specific DNA-me	1.05e+00
28	107	2.2	493	11	S50625	GLO3 protein - yeast	1.05e+00
29	107	2.2	1058	11	S38100	hypothetical protein	1.05e+00
30	107	2.2	1504	11	S51848	hypothetical protein	1.05e+00
31	107	2.2	1758	12	S57015	probable purine nucl	1.05e+00
32	107	2.2	1758	12	S50349	retinol-binding prot	3.70e+00
33	102	2.1	134	7	A29065	glycine-rich protein	7.69e+00
34	99	2.1	203	3	J01061	hypothetical protein	3.70e+00
35	102	2.1	281	10	D30191	bone sialoprotein pr	6.04e+00
36	100	2.1	320	5	GEPTS	peridinin-chlorophyl	6.04e+00
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38	102	2.1	378	9	S47818	NTA monooxygenase co	4.73e+00
39	101	2.1	453	16	I40750	alpha-amylose (EC 3.	6.04e+00
40	99	2.1	482	10	S31478	RNA helicase dbp2 -	6.04e+00
41	100	2.1	550	11	S14048	exed protein - Aerom	6.04e+00
42	100	2.1	678	9	S46953	exed protein - Aerom	6.04e+00
43	100	2.1	678	9	I39678	sericinB - silkworm	2.89e+00
44	103	2.1	1217	12	S52714	sericinB - silkworm	2.89e+00
45	100	2.1	3759	12	A35085	trithorax protein -	6.04e+00

ALIGNMENTS

RESULT 1
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meningitidis (strain M982)
ORGANISM #formal_name Neisseria meningitidis
DATE 03-May-1994 #sequence_revision 03-May-1994 #text-change
23-Aug-1996

ACCESSIONS JN0820: P0635; S33155
REFERENCE JN0818

#authors Legrain, M.; Mazari, V.; Irwin, S.W.; Bouchon, E.;
Quentin-Millet, M.J.; Jacobs, E.; Schuyvers, A.B.
Gene (1993) 130:73-80

#title Cloning and characterization of Neisseria meningitidis genes
encoding the transferrin-binding proteins Tbp1 and Tbp2.

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#status nucleic acid sequence not shown

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#residues 1-711 #label LEG

#cross-references EMBL:215130
#accession P0635

#molecule_type protein
#residues 21-33;58-65;144-161;178-190;419-424 #label LEI

GENETICS

#gene tbp2
#superfamily transferrin receptor

KEYWORDS iron transport; membrane protein; metal binding; receptor
FEATURE 1-20
#domain signal sequence #status predicted #label SIG
#product transferrin-binding protein 2 #status predicted
#label MAT

SUMMARY #length 711 #molecular_weight 76928 #checksum 7833

Query Match 100.0%; Score 4803; DB 7; Length 711;
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Matches 711; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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|||||
1 MNPLVNOAAVLPVFLLSAAGGGSPFLDSVTEPRPKYQDVSSERPOAKQDGG 60
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SEQ ID NO: 2

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DB 301 dggfignrtngfatacdkneketklhpfvdsdsslsqgffgpggeelgffisddqvay 360
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DB 361 vgsaktckdhlengaaasgtgaasgaagtsensakltvldaveltlndkklklnldnf 420
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Query Match 25.2% Score 1208; DB 16; Length 216;
Best Local Similarity 86.1%; Pred. No. 3, 11e-19;
Matches 179; Conservative 14; Mismatches 15; Indels 0; Gaps 0;

```

```

DB 68 1p1peasessngnngngngtataftrkldhtpsedkxadagagtcngasatagdn 127
OY 433 IPLLPRDSSSGMTQADKNGGTEFRKREHTPESSDKXDAAGTQNGQTSNTRAGDN 492
DB 128 gktkyevevccsnllykygmlltrknskaagsgagsgadakevqgsmflgertd 187

```

```

OY 493 GKTKTYEVEVCCSNLTYKGMLLTRKNSKAMQAGNSGADAKTEOVESMFLQGERD 552
DB 188 ekelpseqlvyrsgwyghlaasstwsa 215
OY 553 EKELPTDQNVYRGSWYGHLANGTSWSG 580

```

```

RESULT 3
ENTRY 3
TITLE 3
ORGANISM 3
DATE 3
#accession 3
#status 3
#residues 3
#cross-references 3
#length 210 #molecular-weight 22075 #checksum 6596
SUMMARY 3

```

```

Query Match 25.0% Score 1202; DB 16; Length 210;
Best Local Similarity 86.7%; Pred. No. 4, 0.2e-190;
Matches 182; Conservative 9; Mismatches 19; Indels 0; Gaps 0;

```

```

DB 1 ngavassggtgaarsngaaqssensakltvldaveltlndkklklnldnfnaaqlvvdg 60
OY 372 NGAASSGSGTGAARSGAAQSSSENSKLTTLVLDAVELTLNDKKIKLNLDNFSNAQLVVDGI 431
DB 61 mlp1p1peasesskngangtngtataftrklnhtpsdektdagtaengnpaasntagda 120
OY 432 MLP1P1PEASSSKNGANGTNGTATFTRKLNHTPSDEKTDAGTAENGPAASTAGDA 120
DB 121 ngkkyevevccsnllykygmlltrknskaagsgagsgadakevqgsmflgertd 180
OY 492 NGKTYEVEVCCSNLTYKGMLLTRKNSKAMQAGNSGADAKTEOVESMFLQGERD 551
DB 181 dekeipndqnvvyrgswyghlangtswasn 210
OY 552 DEKEIPTDQNVYRGSWYGHLANGTSWSGN 581

```

```

RESULT 4
ENTRY 4
TITLE 4
ORGANISM 4
DATE 4
#accession 4
#status 4
#residues 4
#cross-references 4
#length 213 #molecular-weight 22751 #checksum 6:64
SUMMARY 4

```

```

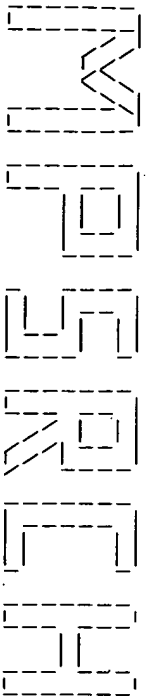
Query Match 22.1% Score 1062; DB 16; Length 213;
Best Local Similarity 81.4%; Pred. No. 3, 0.0e-164;
Matches 162; Conservative 14; Mismatches 21; Indels 2; Gaps 2;

```

```

DB 68 1p1peasessngnngngngtataftrkldhtpsedkxadagagtcngasatagdn 127
OY 433 IPLLPRDSSSGMTQADKNGGTEFRKREHTPESSDKXDAAGTQNGQTSNTRAGDN 492
DB 128 gktkyevevccsnllykygmlltrknskaagsgagsgadakevqgsmflgertd 187

```



(TM)

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Search: protein - protein database search, using Smith-Waterman algorithm
on: Wed Apr 23 08:11:45 1997; Maspar time 20.67 seconds
Tabular output not generated. 826.086 Million cell updates/sec

Title: >US-08-591-447-4
Description: (1-599) from US08591447.pep
Perfect Score: 4134
Sequence: 1 MNPLVNGAAMVLPVFLLSA.....EGKQKASVFGAKRQOLVQ 599

Scoring table: PAM 150
Gap 11

Searched: 89912.segs, 2850787 residues
Post-processing: Minimum Match 0%
Listing first 45 summaries

Database:

plf50
1:ann1 2:ann2 3:ann3 4:ann4 5:unann1 6:unann2 7:unann3
8:unann4 9:unann5 10:unann6 11:unann7 12:unann8
13:unann9 14:unann10 15:unann16:unrev

Statistics: Mean 48.932; Variance 106.796; scale 0.458

Pred. No. is the number of results predicted by chance to have a
score greater than or equal to the score of the result being printed,
and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Match	Query Length	DB ID	Description	Pred. No.
1	4134	100.0	599	7 JN0818	transferrin-binding	0.00e+00
2	1147	27.7	593	9 B44796	transferrin-binding	5.50e-186
3	1147	27.7	593	9 S27483	transferrin-binding	5.50e-186
4	796	19.3	547	9 S49814	transferrin-binding	1.56e-119
5	782	18.9	547	9 A44796	transferrin-binding	6.54e-117
6	777	18.8	625	9 D64107	transferrin-binding	5.64e-116
7	766	18.5	711	7 JN0820	transferrin-binding	6.42e-114
8	757	18.3	547	9 S49815	transferrin-binding	3.08e-112
9	185	4.5	213	16 S61545	transferrin-binding	1.99e-11
10	171	4.1	217	16 S61546	transferrin-binding	2.31e-09
11	167	4.0	210	16 S61548	transferrin-binding	8.77e-09
12	158	3.8	216	16 S61545	transferrin-binding	1.69e-07
13	142	3.4	216	16 S61544	transferrin-binding	2.74e-05
14	112	2.7	41	7 S37626	transferrin-binding	1.81e-01
15	111	2.7	714	11 S66599	hypothetical protein	2.37e-01
16	108	2.6	827	10 F64512	hypothetical protein	5.31e-01
17	104	2.5	250	11 S61626	hypothetical protein	1.52e+00
18	104	2.5	300	8 J00707	methanol oxidation p	1.52e+00
19	105	2.5	351	11 S34261	nodulin-45 - narrow	1.17e+00
20	104	2.5	452	12 S53906	YMK1 protein - yeast	1.52e+00
21	103	2.5	562	11 S57083	chaperonin Tcp1 eps1	1.96e+00

22	104	2.5	863	12 S37040	parmyosin - tapewor	1.52e+00
23	103	2.5	4639	7 A54794	dynamin heavy chain,	1.96e+00
24	98	2.4	176	5 S00636	iron sulfur protein	6.95e+00
25	98	2.4	293	5 J00380	proteinase T (EC 3.4	6.95e+00
26	98	2.4	317	9 S10362	flagellar hook-assoc	6.95e+00
27	98	2.4	333	10 D64317	hypothetical protein	6.95e+00
28	99	2.4	407	11 S08070	cell division contro	5.42e+00
29	98	2.4	411	9 E64088	ATP-dependent protea	6.95e+00
30	100	2.4	513	5 A35742	analysin (EC 3.4.21	4.22e+00
31	98	2.4	786	8 S28084	env polyprotein - si	6.95e+00
32	101	2.4	956	6 S40304	phosphoenolpyruvate	3.28e+00
33	100	2.4	1318	4 HIBP7	internal virion prot	4.22e+00
34	94	2.3	180	5 S58619	NMDH dehydrogenase (1.84e+01
35	94	2.3	286	11 J02289	floral homeotic gene	1.84e+01
36	95	2.3	400	11 S54642	glycine cleavage T p	1.45e+01
37	95	2.3	437	11 S01828	37K protein precursor	1.45e+01
38	97	2.3	505	10 S05357	hypothetical protein	8.89e+00
39	95	2.3	528	1 TVFV9	protein-tyrosine kin	1.45e+01
40	95	2.3	541	1 TVCHS	protein-tyrosine kin	1.84e+01
41	94	2.3	541	5 S31645	protein-tyrosine kin	1.84e+01
42	96	2.3	543	1 TVHVS	protein-tyrosine kin	1.14e+01
43	96	2.3	845	1 A40016	protein 3 - rat	1.14e+01
44	97	2.3	959	11 B44402	nuclear pore complex	8.89e+00
45	95	2.3	2201	13 A54774	ATP binding cassette	1.45e+01

ALIGNMENTS

RESULT 1
ENTRY JN0818 #type complete
TITLE transferrin-binding protein 2 precursor - Neisseria meningitidis (strain B16B6)
ORGANISM #formal_name Neisseria meningitidis
DATE 03-May-1994 #sequence_revision 03-May-1994 #text_change 23-Aug-1996
ACCESSIONS JN0818: P06633; S33153
REFERENCE JN0818
#authors Legrain, M.; Mazarin, V.; Iwain, S.W.; Bouchon, E.; Gentilin-Millet, M.J.; Jacobs, E.; Schryvers, A.B.
#journal Gene (1993) 130:73-80
#title Cloning and characterization of Neisseria meningitidis genes encoding the transferrin-binding proteins Tbp1 and Tbp2.

#accession JN0818
#status nucleic acid sequence not shown
#molecule_type DNA
#residues 1-599 #label LEG
#cross-references EMBL:Z15129
#accession P06633
#molecule_type protein
#residues 21-34/51-61;158-171;351-361;363-368;378-386;441-456;
564-582 #label LEL

SEQIDNO:4

GENETICS
#gene tdb2
CLASSIFICATION #superfamily transferrin receptor
KEYWORDS iron transport; membrane protein; metal binding
FEATURE
1-20
21-599
#domain signal sequence #status predicted #label SIG
#product transferrin-binding protein 2 #status predicted
#label MAT

SUMMARY
#length 599 #molecular-weight 65468 #checksum 382

Query Match 100.0%; Score 4134; DB 7; Length 599;
Best Local Similarity 100.0%; Pred. No. 0.00e+00;
Matches 599; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

DB 1 mnplvngaaamyprvllsaclggsgsfldsvetqdmhsprkyedeksgesqgdvve 60
1 MNPLVNGAAMVLPVFLLSACLGSGSFDLSVETQDMHSRKYEDKSGPESQGDVSE 60
DB 61 nsaaaygfvavkxiprrahfnprkyekhpilgsmcwklgrgpnstferdelekrgsse 120
61 NSAAAYGFVAVKLPRRAHFNPRKYEKHPILGSMCKWLGRGPNSTFERDELEKRGSSSE 120

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Db 121 11estwedgqsrwvgytftvyrsgvyvlnknidknmivlfspdgyllykqkpskel 180
Oy 121 11ESMEWEGOSRWVGYTFTVYRSQVYVLNKNIDKNMIVLFGPDGYLYYKQKPSKEL 180
Db 181 psekltvgytdvyrdaekqrfeeglsgaagdgkgsalaleegvlylrqaeasgthtdfg 240
Oy 181 pSEKltvgytdvyrdaekqrfeeglsgaagdgkgsalaleegvlylrqaeasgthtdfg 240
Db 241 mtsefvedfscdkltklylrnmrltqnsenkqklttlytqatlhgrfyskakaadkx 300
Oy 241 MTSEFVEDFSCKLTklylrnmrltqnsenkqklttlytqatlhgrfyskakaadkx 300
Db 301 atngshpfsisdslleggyfypkgeelagkflsndkvaavfgakqkdkdgmaaspat 360
Oy 301 ATNGSHPFISDSLSLEGGFYPKGEELAGKFLSNDKVAAVFGAKQKDKDGMASGPAT 360
Db 361 etvldayrltgeefkkgelidfgdvkkllydvvelslpsegnkaafhelegngvaktv 420
Oy 361 ETVLDAYRLTGEEFKKGELIDFGDVKKLlydvvelslpsegnkaafhelegngvaktv 420
Db 421 ccenldymsgfjlskenkddmflqvrtpvsvdaarteanaakyrqvyqlyangtswage 480
Oy 421 CCSNLDYMSGFJLSKENKDDMFLQVTRTPVSDVAARTEANAAKYRQVYQLYANGTSWAGE 480
Db 481 asngegnrfevdftsklsgtltakdtspaflltamkdnngfsgvaktgengfald 540
Oy 481 ASNGEGNRFEVDFTSKlsgtltakdtspaflltamkdnngfsgvaktgengfald 540
Db 541 pmtgnashyhlteavsgfygknaemggsfsfpgnappegkgaavvfgakqqlvq 599
Oy 541 PMTGNASHYHLEAVSGFYGKNAEMGGSFSFPGNAPPEGKGAAVVFGAKQQLVQ 599

```

RESULT 2

ENTRY B44796 #type complete
TITLE transferrin-binding protein, Tfba - Actinobacillus
ORGANISM pleuropneumoniae
DATE 24-Mar-1993 #sequence_revision 18-Nov-1994 #text_change 18-Nov-1994

ACCESSIONS B44796
REFERENCE A44796
#authors Gerlach, G.F.; Klashinsky, S.; Anderson, C.; Potter, A.A.;
#journal Infect. Immun. (1992) 60:3253-3261
#title Characterization of two genes encoding distinct
transferrin-binding proteins in different Actinobacillus
pleuropneumoniae isolates.
#cross-references MVID:92347999
#contents AP37, serotype 17
#accession B44796
#status preliminary
#molecule_type DNA
#residues 1-593 #label GER
#cross-references NCBI:109737; NCBI:109738
#note sequence extracted from NCBI Backbone
SUMMARY #length 593 #molecular_weight 65529 #checksum 2440

Query Match 27.7%; Score 1147; DB 9; Length 593;
Best Local Similarity 38.3%; Pred. No. 5,50e-186;
Matches 237; Conservative 153; Mismatches 176; Indels 53; Gaps 38;

Db 1 mbfkl-nyalafstflvacsgkgsfledvyrpnqtaekattsygdeetkkktkee 59
Oy 1 MNNPLVNOAAMVLPVFLSLACGGGSGFDLSEVTVQDMHS-KPK--YEDKESQPSOOD 57
Db 60 ldklnepalgyetqlirtnkapktetgekrnervelsedkltkiygesvevlphldeln 119
Oy 58 VSENGAAGFAVVKLPBRNAHNPYKKEKH-KPLGSM-DWK--KIQRGEPNFSERDELE 113
Db 120 gktctndvyns--hsk-lidknrdlkyrsgvyvysgfneirndsgfhwfkgldgyv 176
Oy 114 KRGSSELESMEWEGOSRWVGYTFTVYRSQVYVLNKNIDKNM-IVLF--GPDGYL 169

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Db 177 yylgvtpekselpkgyvlykgtwdfvsnlnlere-ldgfdtsqdg-kvsvatsilevnr 234
Oy 170 YKKGPEPSKELEPSEK-IYKGTWDFVTD-AMEKQFEGLGSAAGDGKGSALALEEGLR 227
Db 235 dhkvekldgdevkvanssefawdfdkkltgslryrnylnrnkaq--ev-ckyslea 291
Oy 228 NQAEASS-GHDF-GMT--SEFVDFSDKTLGTYRNRRTOONNSEKKQIKTRTYTQA 283
Db 292 diagrffgka-kaek-a--gd-plfidsnyleggyfypkaeemagkftfnkalfaufa 346
Oy 284 TLHGKRFKALADKGAATNGSHPFISDSLSLEGGFYPKGEELAGKFLSNDKVAAVFG 343
Db 347 ak-se--nge--t-terlidatklitqfnakelnmfgaavlyldgqkidi-avgnf 398
Oy 344 AKQDKKDGEMAAPATETVDAVRITGEFEKKQIDISFGDVKKLVDVVELSLPSEGN 403
Db 399 knsktvelngktmvaavacsenleymkfgqlwqkegkqgvdnslflggetatckma-- 456
Oy 404 KAARQHELEONGVAKATVCCSNLDYMSFGKL-SKE-N--KDD-WFLOGVTRPVSDVART 457
Db 457 ggnvykyvtdavlskgtwnvlaeaddnrresgyrtefdvnsdkkvnngkldkgyvnpvft 516
Oy 458 EANAkyrgtvygytANGTSWGEA-SNQGEGNRAEPVDESTKKSISTTLAKORTSPAT 516
Db 517 vdatlngngfsgktsdgsfaldagssqbnnavfsdkvngsfygpftagelggqfh-h- 574
Oy 517 ITAMIKONGSGVAKGENSEFALDPONTGNSHYTHIEATVSGGFYKNALEMGSFSFG 576
Db 575 ksdngs---vgavfgakrq 590
Oy 577 NAPEGKQEKASVVFAGAKRQ 595

```

RESULT 3

ENTRY S27483 #type complete
TITLE transferrin-binding protein - Actinobacillus pleuropneumoniae
ORGANISM pleuropneumoniae
DATE 06-Jan-1995 #sequence_revision 06-Jan-1995 #text_change 06-Jan-1995

ACCESSIONS S27483
REFERENCE S27483
#authors Gerlach, G.F.; Klashinsky, S.; Anderson, C.; Potter, A.A.;
#submission submitted to the EMBL Data Library, March 1992
#description Characterization of an Actinobacillus pleuropneumoniae
transferrin-binding protein and its distribution among type
strains.
#accession S27483
#status preliminary
#molecule_type DNA
#residues 1-593 #label GER
#cross-references EMBL:M85274
SUMMARY #length 593 #molecular_weight 65582 #checksum 2644

Query Match 27.7%; Score 1147; DB 9; Length 593;
Best Local Similarity 38.4%; Pred. No. 5,50e-186;
Matches 238; Conservative 152; Mismatches 176; Indels 53; Gaps 39;

Db 1 mbfkl-nyalafstflvacsgkgsfledvyrpnqtaekattsygdeetkkktkee 59
Oy 1 MNNPLVNOAAMVLPVFLSLACGGGSGFDLSEVTVQDMHS-KPK--YEDKESQPSOOD 57
Db 60 ldklnepalgyetqlirtnkapktetgekrnervelsedkltkiygesvevlphldeln 119
Oy 58 VSENGAAGFAVVKLPBRNAHNPYKKEKH-KPLGSM-DWK--KIQRGEPNFSERDELE 113
Db 120 gktctndvyns--hsk-rldknrdlkyrsgvyvysgfneirndsgfhwfkgldgyv 176
Oy 114 KRGSSELESMEWEGOSRWVGYTFTVYRSQVYVLNKNIDKNM-IVLF--GPDGYL 169
Db 177 yylgvtpekselpkgyvlykgtwdfvsnlnlere-ldgfdtsqdg-kvsvatsilevnr 234

Application No.: 591,447**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: A copy of the "Sequence Listing" in computer readable form has been submitted. However, the specification contains sequences not submitted as a copy of the "Sequence Listing" in computer readable form or as a paper copy.

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

For PatentIn software help, call (703) 308-6856

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